CR: Complete remission; DOD: Died of disease; MA: Myeloablative; NMA: Non-myeloablative; MSD: matched sibling donor; MRD: matched related donor.

151

OUTCOMES AFTER CD34+ SELECTION WITH OR WITHOUT THE ADDITION OF PHOTO-ALLODEPLETED T LYMPHOCYTES IN MYELOABLATIVE HLA-MATCHED SIBLING TRANSPLANTATION

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Introduction: Photodepletion (PD) is a method to selectively deplete alloreactive lymphocytes from the graft to reduce graft versus host disease (GVHD) in allogeneic stem cell transplantation. We have previously reported results with PD and shown a low rate of relapse without significant GVHD (Mielke, et al. and McIver, et al. BBMT 2011). In this retrospective analysis, we compared transplants using photodepleted donor lymphocytes (n = 24) with a similar cohort of T cell depleted (TCD) transplants (n = 48).

Methods: All subjects received myeloablative conditioning with cyclophosphamide (120 mg/kg), fludarabine (125 mg/m^2) and TBI (12 Gy, or 4 Gy for age ≥55). Peripheral blood stem cells were CD34+ selected by the Miltenyi CliniMacs system, with infusion of a target CD34+ dose of 6 x 10^6/kg (range 3-10 x 10^6/kg) and a CD3+ dose of <5 x 10^4 /kg. All patients received cyclosporine as the only GVHD prophylaxis. The PD cohort received 5 x10^6/kg PD donor lymphocytes at day 0 while the TCD cohort received an unmanipulated DLI of 5 x10^6 CD3+/kg on day 90.

Results: Seventy-two patients underwent HLA-identical sibling transplant. The median age was 43 years (range 16-68), 50% were males. Transplant indications were AML (29), ALL (17), biphenotypic acute leukemia (2), MDS/MPD (15), CML (3), NHL/CLL (6). Baseline characteristics were similar apart from a greater proportion of high risk patients in the PD cohort (66% vs 50%).

The time to ANC >0.5 x 10^9/L and the time to complete donor myeloid chimerism (median, day 14) were similar in both groups, but PD transplants achieved earlier complete donor T-lymphocyte engraftment (31 vs 45 days, p = 0.01). Primary engraftment failure was seen in 3 patients receiving TCD versus none in the PD cohort. There were no significant differences in other clinical outcomes. The cumulative incidence of acute grades II-IV GVHD, III-IV GVHD, chronic-limited GVHD and chronic-extensive GVHD were 50% vs 46%, 13% vs 18%, 39% vs 12% and 26% vs 33% respectively, in PD vs TCD cohorts. With a median follow up of 2.8 years, Kaplan-Meier estimates of overall survival, relapse and nonrelapse mortality were 44%, 28% and 46% respectively for PD and 49%, 25% and 35% for TCD.

Conclusions: This comparison shows that the addition of 5x10^6/kg photodepleted donor lymphocytes at day 0 to a CD34+ selected peripheral stem cell graft results in superior engraftment, equivalent low rates of GVHD and equivalent disease control in HLA-matched sibling transplantation.

152

GRANULOCYTE TRANSFUSIONS IN A PATIENT WITH APLASTIC ANEMIA SUFFERING FROM LIFE-THREATENING FUNGAL INFECTION – GAPPING FOR HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Acquired aplastic anemia (AA) is the most common form of bone marrow failure. It is a life-threatening condition accompanied by severe infections, including several fungal specious. Among these, fusarium is emerging pathogen in immunocompromized patients, particularly those with severe and prolonged neutropenia. Allogeneic hematopoietic cell transplantation (HCT) is the treatment of choice for AA in patients with matched sibling donor.

Patient and Methods: One year old child was diagnosed as suffering from acquired AA. Due to lack of matched related donor, he received treatment with cyclosporine-A and anti-thymocytic globulin (ATG). While being neutropenic, he developed disseminated life-threatening fusarium fungal infection including positive blood culture, multiple skin lesions and osteomyelitis. The patient received amphotericin-B with no clinical improvement and general deterioration. In order to save the patient's life and prepare him for future transplant, he received 12 granulocyte transfusions over a period of 3 months. Granulocytes were harvested from adult volunteers using granulocyte-colony-stimulating-factor (G-CSF) and dexamethasone. Every harvest was divided into 2 doses given every 12 hours.

Results: Skin lesions disappeared, blood cultures became negative and osteomyelitis resolved during granulocyte transfusions. By that time a new sibling was born, from whom cord blood was harvested and HLA examination revealed matched sibling donor. Since the fusarium disseminated infection was controlled the patient was able to undergo allogeneic HCT using ATG (Fresenius, 5mg/kg/day for 5 days) and cyclophosphamide (50mg/kg/day for 4 days) as conditioning regimen. Neutrophil engraftment occurred on day +14 with donor chimerism between 80-90%. No veno-oclusive-disease (VOD) or graft-versus-host-disease (GVHD) was demonstrated. He is currently 140 days post transplant alive and well with no evidence for the fusarium infection.

Conclusions: Granulocyte transfusions by G-CSF-stimulated donors while waiting HCT should be considered in patients suffering from life-threatening fungal infections.

153

Stemex® IS EXPANDING: PIVOTAL TRIAL NEARS COMPLETION, AND DEVELOPMENT OF A CRYOPRESERVED PRODUCT IS UNDERWAY

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Cord blood transplantation (CBT) is limited by low number of TNC and CD34+ cells, influencing the incidence and rate of hematopoietic recovery and risk of early transplant-related mortality. Ex vivo expansion is a strategy to increase the number of progenitor cells and improve clinical outcomes. Several early stage studies are evaluating the clinical benefit of expansion, mainly in a double CBT configuration. The StemEx® trial evaluates the potential contribution of expansion in a single CBT configuration. StemEx is manufactured from a portion of a single CBU, originally frozen in 2 separate fractions. CD133+ progenitor cells, purified from the smaller or equal fraction, are cultured for 21-23 days with cytokines and a copper chelator, TEPA, which delays differentiation and promotes expansion of progenitor cells with engraftment capabilities. A global pivotal registration study evaluating the safety and efficacy of StemEx in patients with hematological malignancies following myeloablative treatment is currently completing recruitment. Safety and efficacy outcomes of the study will be available in 2012. To date, 82 of 88 StemEx batches manufactured in 3 centralized GMP facilities, have been successfully expanded: median fold expansion of TNC, CD34+ cells and CFU over culture input were 399 (range 52-764), 75 (6-280) and 107 (43-662), respectively. Expansion of only a portion of the CBU resulted in a median 8.4 fold increase (0.8-90.3) in the number of CD34+ cells infused over the number that would be infused from the entire CBU without expansion. The CFU potential of culture seeded CD133+ cells measured at day-0 of production indicates the expansion potential of the cryopreserved CB cells. In all six batches which failed to expand, day-0 CFU was low, while day-0 CFU of all successfully expanded batches was within specification ranges. This information, available before patient myeloablation, strengthens the clinical applicability of StemEx. All StemEx batches were successfully delivered and infused. We are currently in the last stages of development of a frozen StemEx product. The added flexibility in the timing of transplantation allows for changes resulting from patient disease progression or complications. With the challenges of an ex vivo expanded product being successfully met in the current registration trial, and the development of a frozen